Regulatory Science Support of Device Innovation

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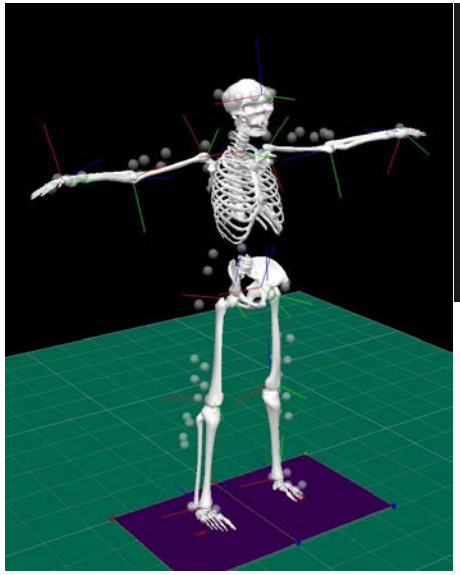
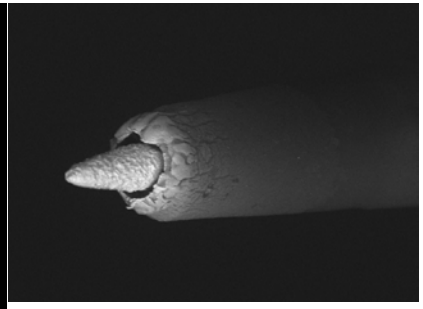
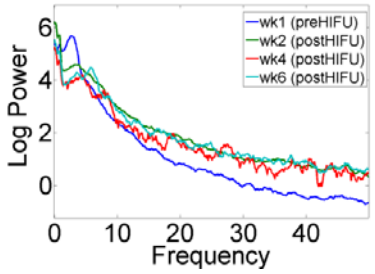
- Regulatory science: the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of FDA-regulated products.- *FDA Regulatory Science Strategic Plan*

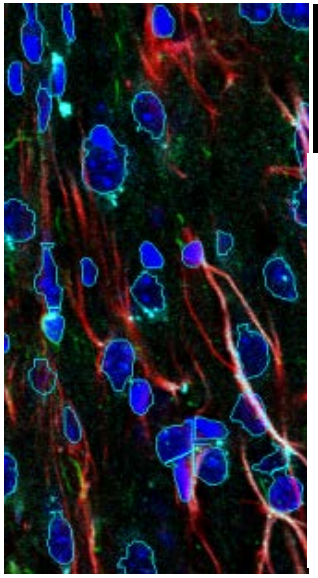
- Test platforms to evaluate long-term safety and reliability of implanted neural electrodes and metrics to characterize system performance

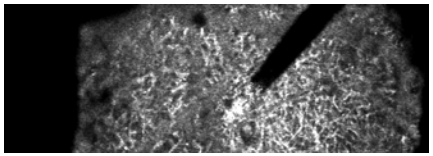
- FDA-DARPA interagency agreement based on common philosophy (Reliable Neural Technology RE-NET and Hand Proprioceptive and Touch Interfaces HAPTIX)

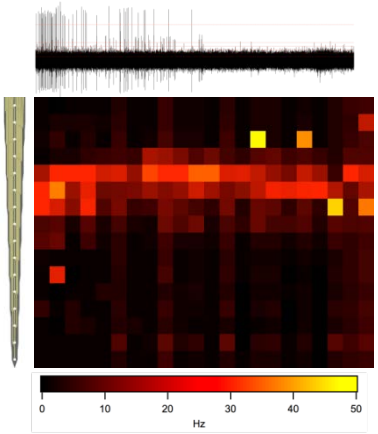










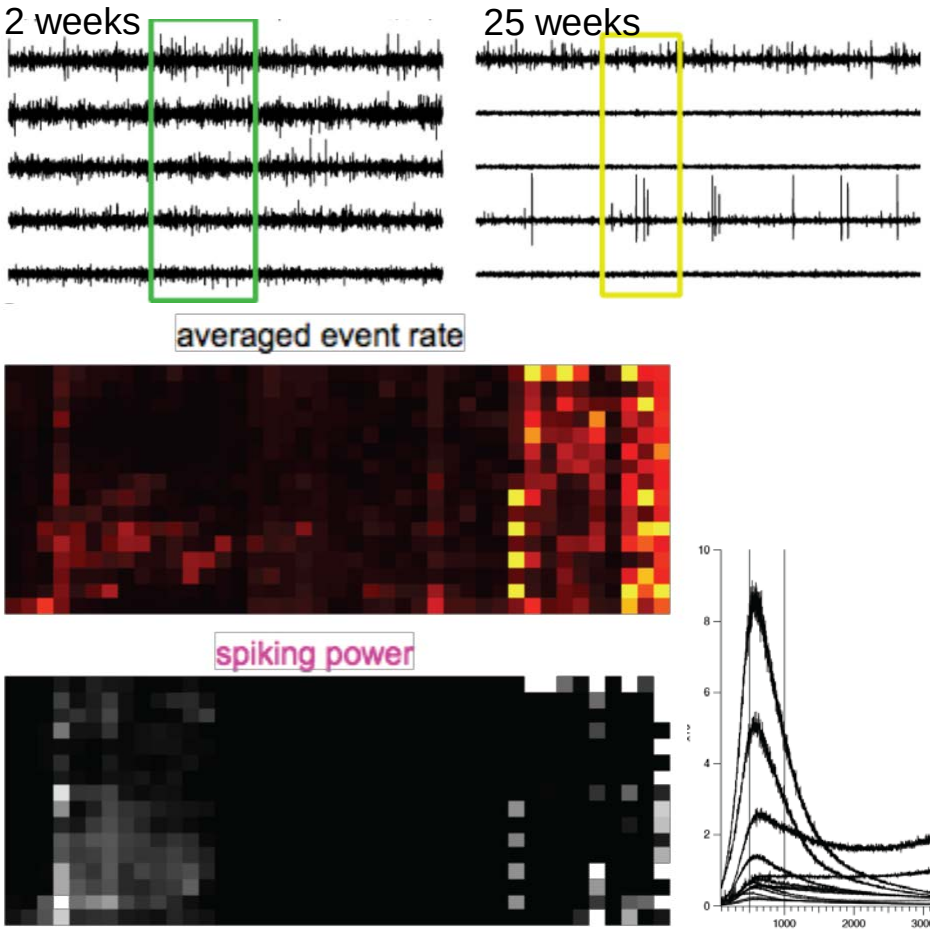


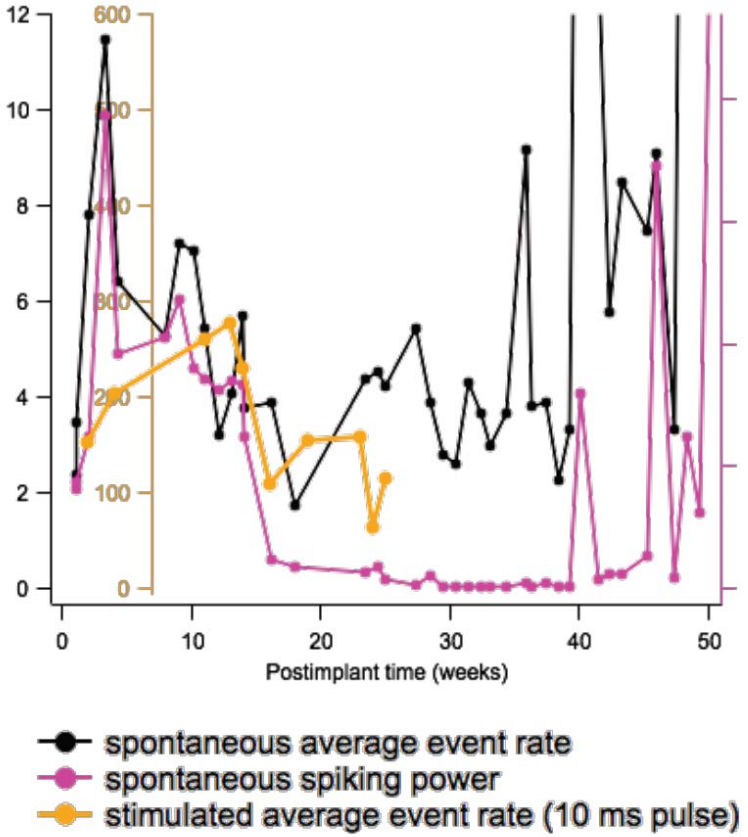
- Human performance
- Neural Implant electrophysiology
- In vitro device testing
- Biomarker development
- Safety and reliability – neural interfaces (PNS, CNS)

- Flexible electronics
- Electrochemical device tissue interface (CLARITY, reactive accelerated aging)
- Bidirectional communication between person and product

Chronic electrophysiology and markers of device failure

- Capturing and measuring neurophysiological data
- Robust, translatable metrics





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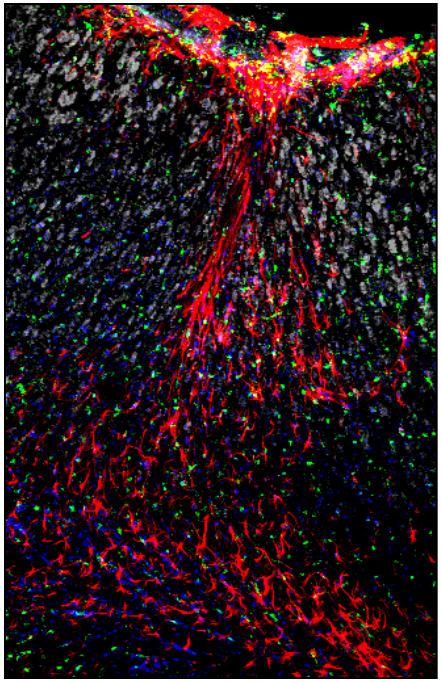
Kelliann Wachrathit
Taylor Hearn

Electrode-tissue interface

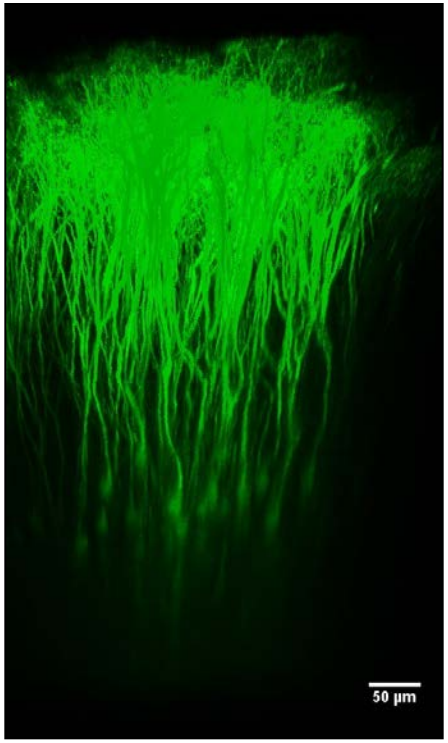
- Neuroinflammation
- Structural re-organization
- Vascular remodeling

Specific to electrode type

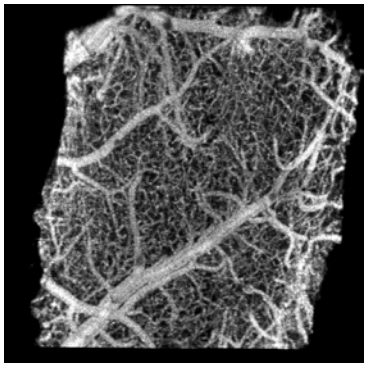


Fixed tissue

In vivo



Day 0



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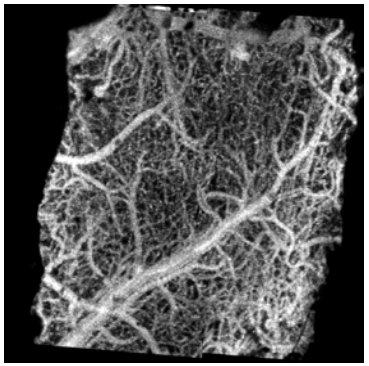
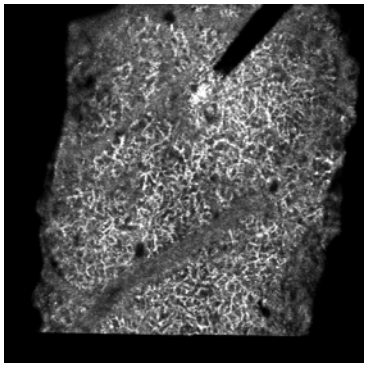
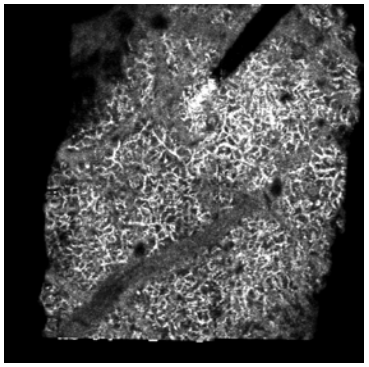
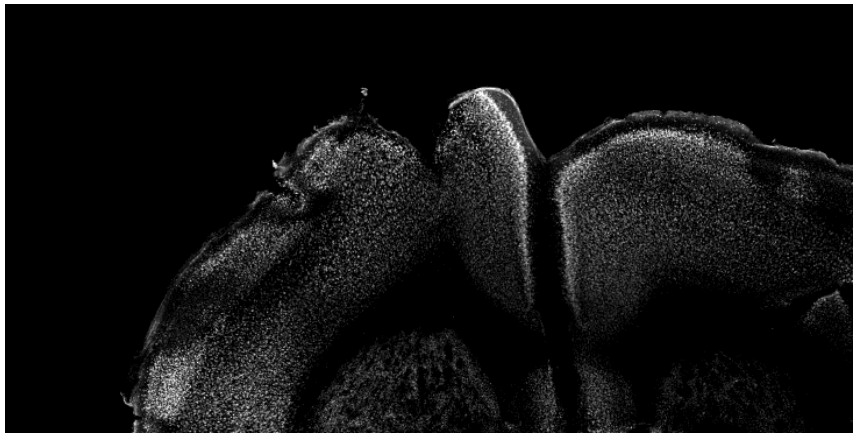




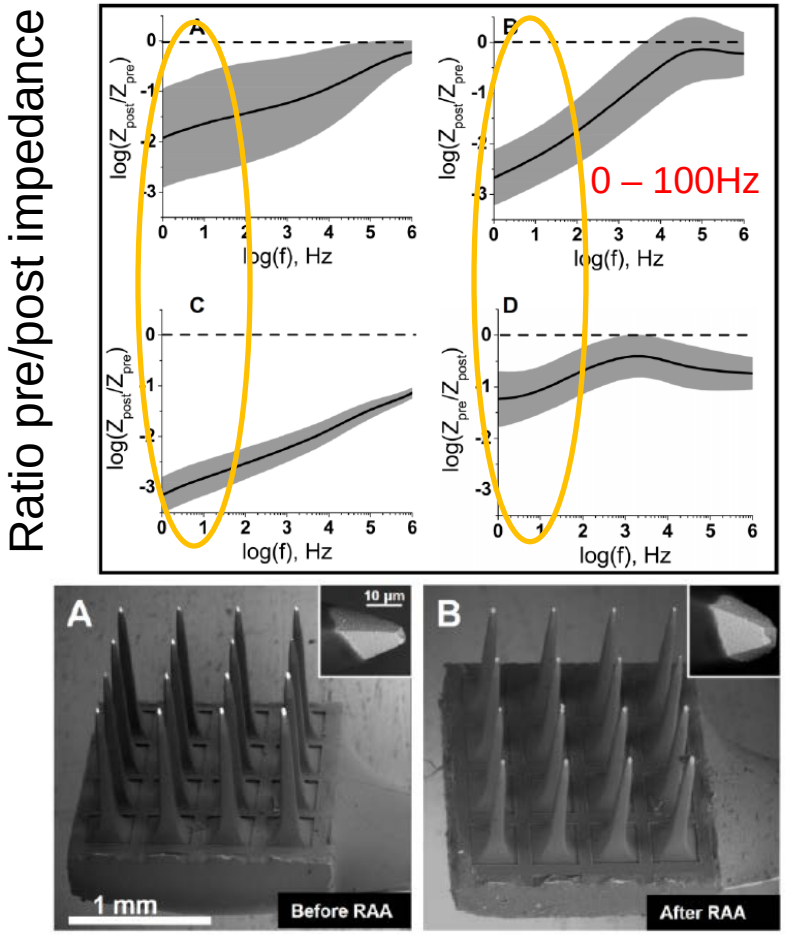




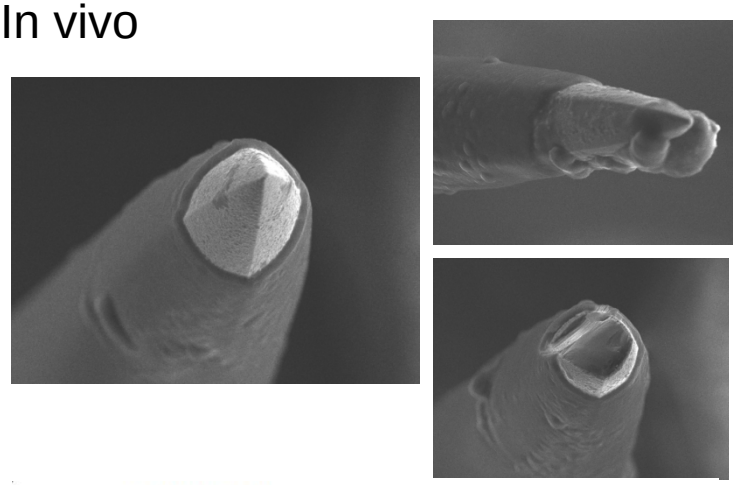
Do-Hyun Kim
Daniel Hammer
Erkinay Abliz
Adam Boretsky
Andrea Lozzi
Anjuli Jain
Kiersten Ruda
Kelliann Wachrathit
Gretchen Knaack

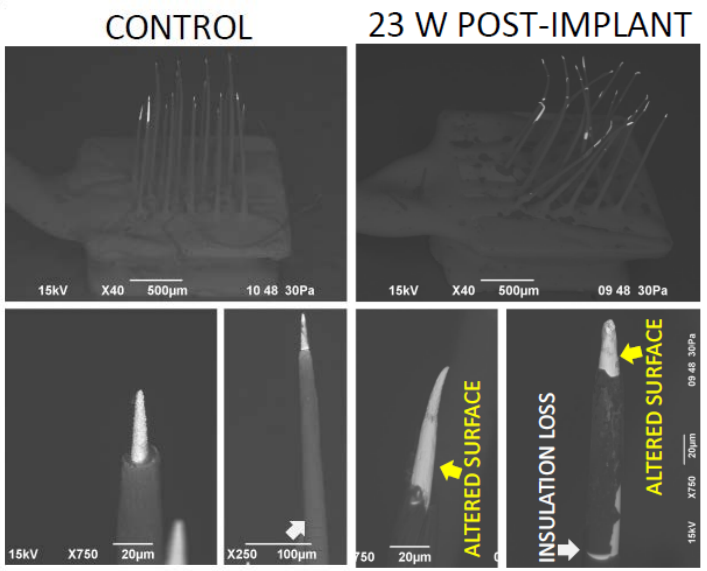
Materials performance

Reactive accelerated aging – in vitro



In vivo



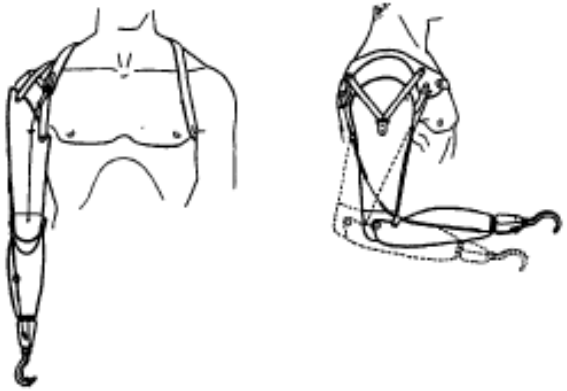


Pavel Takmakov
Kiersten Ruda
Srikanth Vasudevan

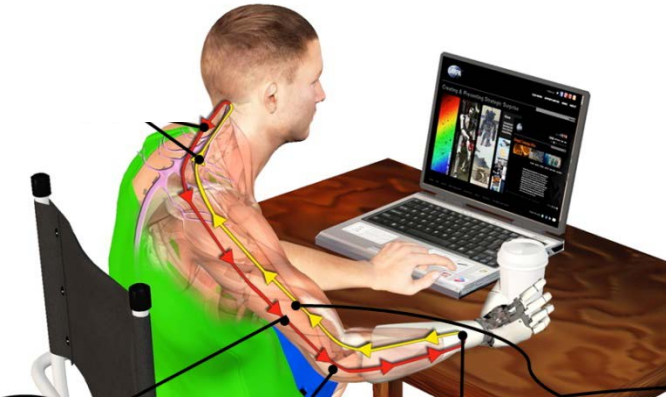
Human performance

Are we prepared to assess performance when scientific progress brings new benefits and risks ?

Technology



PROGRESS



Performance

PROGRESS

Patient-centered, clinically meaningful test methods

How does developing science shape the regulatory pathway for medical devices?

Valid scientific evidence determines safety

"There is reasonable assurance that a device is safe when it can be determined based on valid scientific evidence that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh the probable risks."

21 CFR 860.7

Valid scientific evidence determines effectiveness

"There is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results."

21 CFR 860.7

Valid scientific evidence comes from:

- Well-controlled investigations
- Partially controlled studies
- Objective trials without matched controls
- Self controls
- Historical controls
- Well-documented case histories by qualified experts
- Reports of significant human experience with a marketed device

…from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use.

21 CFR 860.7

Valid scientific evidence: more details

860.7(d)(2) specifically notes the following types of evidence that may be required for safety:

- investigations using laboratory animals
- investigations involving human subjects
- nonclinical investigations including in vitro studies

860.7(e)(2) specifies that well-controlled investigations, as defined in 860.7(f), should be the basis of effectiveness determination unless this is not reasonably applicable to the device. Some alternatives, such as historical controls, are listed in 860.7(c)(2).

21 CFR 860.7

Regulatory definitions of both safety and effectiveness rely on valid scientific evidence.

Valid scientific evidence, such as the kind that supports a marketing application, is produced by nonclinical and clinical research.

Research is also needed to create, critique, and refine the **ways of creating valid scientific evidence**:
in vitro, in vivo, in silico.

This is regulatory science; this is where we can help.

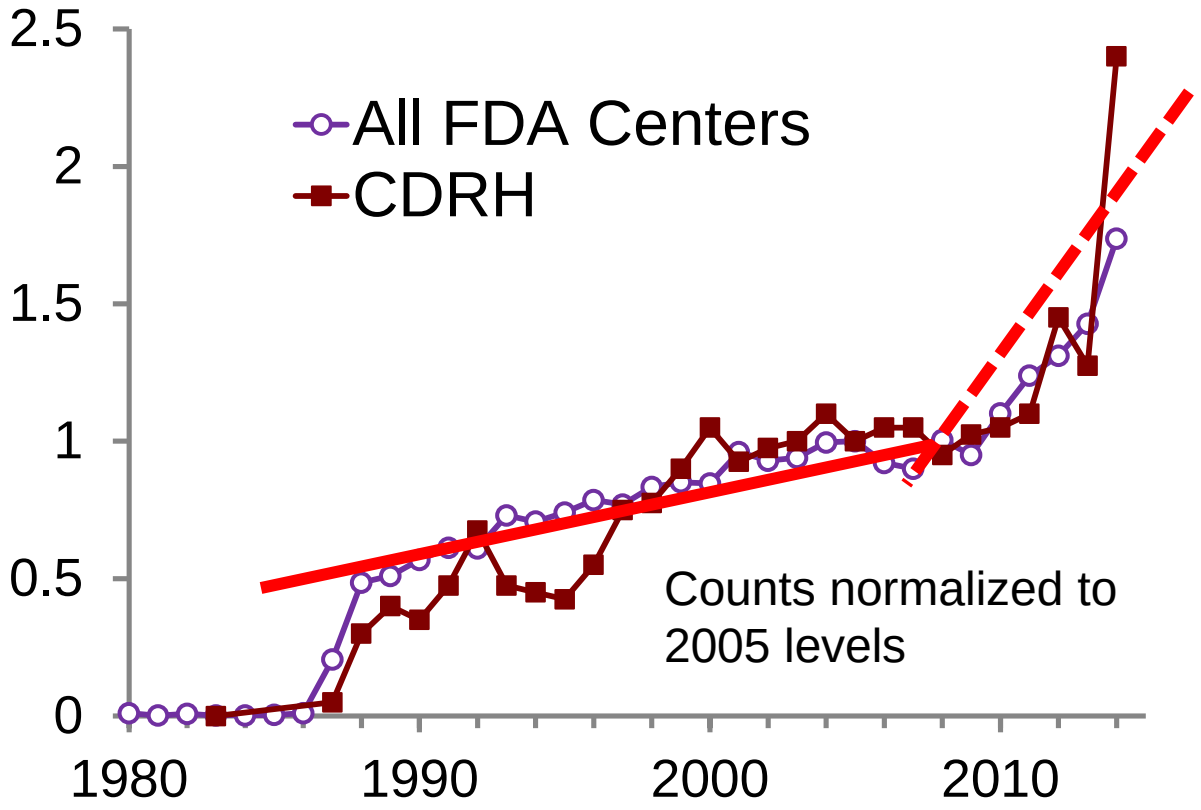
for example…

Evidence for innovative devices requires innovation in regulatory science

Example safety and effectiveness claims…	**…and example of a corresponding regulatory science need**
This brain/nerve implant is safe. →	*Neurotoxicity assays*
This brain/nerve implant will work for X duration. →	*Neural recording/stimulation reliability assays*
These components will work together. →	*Consistent interconnects, standards*
This system will improve the patient's function. →	*Functional outcome measures*

FDA innovation in regulatory science is increasingly visible and collaborative

Citations in PubMed with FDA-affiliated authors, 1980-2014



How do regulatory science research results have an impact?

When they are incorporated into medical device development tool qualification *(currently in pilot phase)*

When sponsors rely on them to produce convincing evidence

When they inform premarket review or postmarket study by CDRH staff

When they are incorporated into guidance

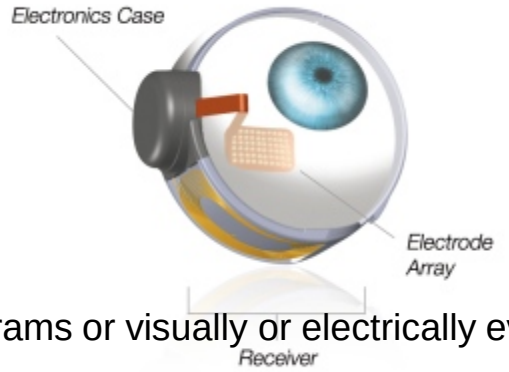
When they are incorporated into standards

Guidance

Guidance documents are documents prepared for FDA staff , applicants/sponsors, and the public that describe the agency's interpretation of or policy on a regulatory issue.

21 CFR 10.115(b)(1)

Investigational Device Exemption (IDE) Guidance for Retinal Prostheses
6 March 2013
Ethan Cohen, OSEL and Bernard Lepri, ODE



"The animal study test reports should include the following items:
…
stimulation levels and rates used (if present),
visually evoked response testing (if present) such as electroretinograms or visually or electrically evoked potentials, and
histology of the eye and retina with particular attention to regions of device implantation or attachment…"

Guidance documents do not include…speeches, journal articles and editorials, media interviews…or other communications directed to individual persons or firms.

21 CFR 10.115(b)(3)

Standards

CDRH believes that conformance with recognized consensus standards can support a reasonable assurance of safety and/or effectiveness for many applicable aspects of medical devices. Therefore, information submitted on conformance with such standards should have a direct bearing on safety and effectiveness determinations…

Guidance on Recognition and Use of Consensus Standards, 17 September 2007

Signal processing	60601-2-47:2012, ANSI AAMI EC57 Heartbeat Detection (ECG) ANSI S3.42-2012/Part 2 Hearing aid signal processing
Data interchange	FDA XML format for electrocardiogram (ECG) data (2003)
Functional outcomes	ASTM WK41469 (***draft***): Clinical trials for hip replacement Measurement of gait speed change is a functional outcome measure for hip replacement surgery.

Pilot program open now!

Medical device development tools

FDA intends to work together with developers of tools … to determine whether certain tools may be developed and qualified in order to facilitate more predictable, efficient, and transparent regulatory evaluation when MDDTs are used to generate valid scientific evidence for medical device premarket applications.

May include:

Clinical outcome assessments

Biomarker tests

Nonclinical assessment models

Other unmet public health needs

Questions? kathryn.ocallaghan@fda.hhs.gov
Submit to MDDT@fda.hhs.gov

Regulatory Science Needs for BCI Devices

Some suggested areas where further scientific development is needed:

- Electrode performance (recording and stimulation)
- Brain/nerve implant toxicity assessment
- Leads and connectors
- Data formats
- Outcome measures (ADLs, alternative trial designs)

"… Although FDA's primary responsibility is to review the safety and effectiveness of new medical products developed by industry, the Agency is also committed to assisting product developers in translating discoveries in basic science into new therapies that will save lives and improve health care."

-FDA Draft Strategic Priorities 2014-2018
http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm402888.htm

Photo: April Bartholomew
The Morning Call
Lehigh Valley, PA
14 October 2014

Get in touch!

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